

WHAT IS CLAIMED IS:

- 1 1. A method for inducing insulin gene expression in cultured
2 endocrine pancreas β -cells, the method comprising the steps of:
3 (i) expressing a recombinant NeuroD/BETA2 polynucleotide and a
4 recombinant PDX-1 polynucleotide in endocrine pancreas β -cells that have been cultured
5 under conditions such that the β -cells are in contact with other cells in the culture; and
6 (ii) contacting the cells with a GLP-1 receptor agonist, thereby inducing
7 insulin gene expression in the β -cells.
- 1 2. The method of claim 1, wherein the GLP-1 receptor agonist is a
2 GLP-1 analog.
- 1 3. The method of claim 1, wherein the GLP-1 receptor agonist has an
2 amino acid sequence of a naturally occurring peptide.
- 1 4. The method of claim 3, wherein the GLP-1 receptor agonist is
2 GLP-1, exendin-3, or exendin-4.
- 1 5. The method of claim 1, wherein the cells are cultured as aggregates
2 in suspension.
- 1 6. The method of claim 1, wherein the β -cells are human β -cells.
- 1 7. The method of claim 1, wherein the β -cells express a recombinant
2 oncogene.
- 1 8. The method of claim 7, wherein the β -cells express more than one
2 recombinant oncogene.
- 1 9. The method of claim 1, wherein the β -cells express a recombinant
2 telomerase gene.
- 1 10. The method of claim 1, wherein the β -cells are β lox5 cells.
- 1 11. A method of identifying a compound that modulates β -cell
2 function, the method comprising the steps of contacting cells made by the method of

3 claim 1 with the compound and determining the effect of the compound on β -cell
4 function.

1 12. A stable culture of endocrine pancreas β -cells, wherein the β -cells
2 are in contact with other cells in the culture, wherein the β -cells express a recombinant
3 PDX-1 polynucleotide and a recombinant NeuroD/BETA2 polynucleotide, and wherein
4 insulin gene expression is stimulated in the β -cells when exposed to an effective amount
5 of a GLP-1 receptor agonist.

1 13. The culture of claim 12, wherein the GLP-1 receptor agonist is a
2 GLP-1 analog.

1 14. The culture of claim 12, wherein the GLP-1 receptor agonist has an
2 amino acid sequence of a naturally occurring peptide.

1 15. The culture of claim 14, wherein the GLP-1 receptor agonist is
2 GLP-1, exendin-3, or exendin-4.

1 16. The culture of claim 12, wherein the cells are cultured as
2 aggregates in suspension.

1 17. The culture of claim 12, wherein the β -cells are human β -cells.

1 18. The culture of claim 12, wherein the β -cells express a recombinant
2 oncogene.

1 19. The culture of claim 18, wherein the β -cells express more than one
2 recombinant oncogene.

1 20. The culture of claim 12, wherein the β -cells express a recombinant
2 telomerase gene.

1 21. The culture of claim 12, wherein the β -cells are β lox5 cells.

1 22. A method of identifying a compound that modulates β -cell
2 function, the method comprising the steps of contacting the culture of claim 12 with the
3 compound and determining the effect of the compound on β -cell function.

1 23. A method of treating a diabetic subject by providing to the subject
2 cells that secrete insulin in response to glucose, the method comprising the step of
3 administering to the subject an effective amount of cells according to claim 1.

1 24. A method of treating a diabetic subject by providing to the subject
2 cells that secrete insulin in response to glucose, the method comprising the steps of:

3 (i) contacting a culture of endocrine pancreas β -cells expressing a
4 recombinant PDX-1 polynucleotide and a recombinant NeuroD/BETA2 polynucleotide
5 with a GLP-1 receptor agonist, wherein the β -cells have been cultured under conditions
6 such that the β -cells are in contact with other cells in the culture; and

7 (ii) administering the β -cells to the subject, thereby providing to the
8 subject cells that secrete insulin in response to glucose.

1 25. The method of claim 24, wherein the diabetic subject is a human.

1 26. The method of claim 25, wherein the subject has Type I insulin
2 dependent diabetes.

1 27. The method of claim 24, wherein the GLP-1 receptor agonist is a
2 GLP-1 analog.

1 28. The method of claim 24, wherein the GLP-1 receptor agonist has
2 an amino acid sequence of a naturally occurring peptide.

1 29. The method of claim 28, wherein the GLP-1 receptor agonist is
2 GLP-1, exendin-3, or exendin-4.

1 30. The method of claim 24, wherein the β -cells are cultured as
2 aggregates in suspension.

1 31. An endocrine pancreas β -cell comprising a recombinant PDX-1
2 polynucleotide and a recombinant NeuroD/BETA2 polynucleotide.

1 32. The β -cell of claim 31, wherein the β -cell is a human β -cell.

1 33. The β -cell of claim 31, wherein the β -cell expresses a recombinant
2 oncogene.

1 34. The β -cell of claim 33, wherein the β -cell expresses more than one
2 recombinant oncogene.

1 35. The β -cell of claim 31, wherein the β -cell expresses a recombinant
2 telomerase gene.